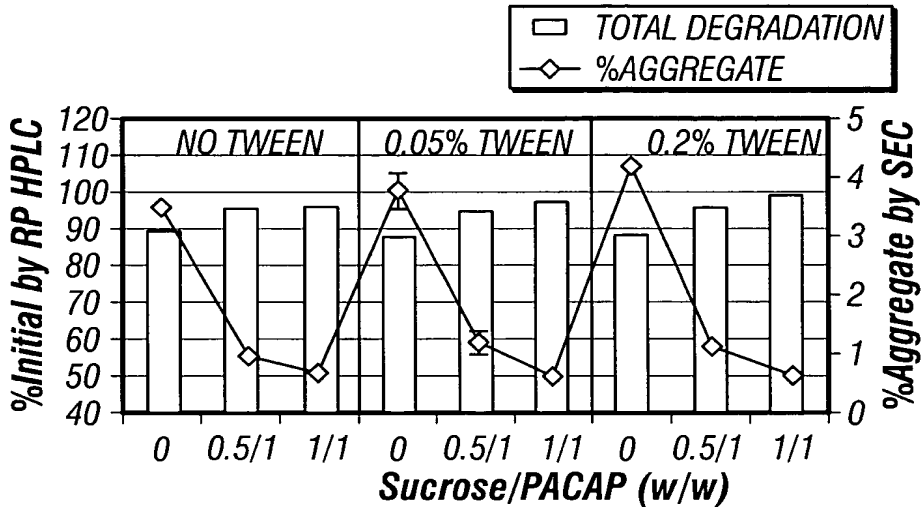
TOTAL DEGRADATION
%AGGREGATE
NO TWEEN
0.05% TWEEN
0.2% TWEEN
%Initial by RP HPLC
%Aggregate by SEC
120
110
100
90
80
70
60
50
40
5
4
3
2
1
0
0
0.5/1
1/1
0
0.5/1
1/1
0
0.5/1
1/1
Sucrose/PACAP (w/w)

FIG. 1

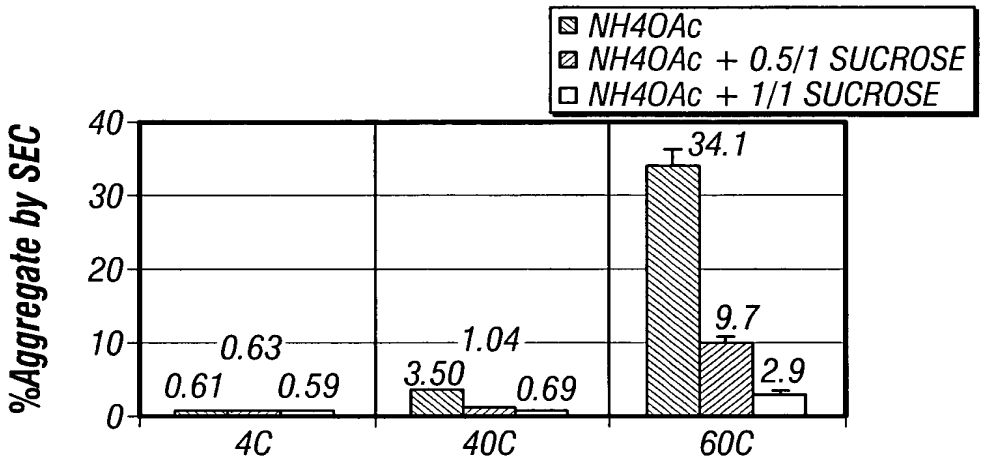
NH4OAc
NH4OAc + 0.5/1 SUCROSE
NH4OAc + 1/1 SUCROSE
%Aggregate by SEC
40
30
20
10
0
0.61
0.59
0.63
3.50
0.69
1.04
34.1
9.7
2.9
4C
40C
60C

FIG. 2

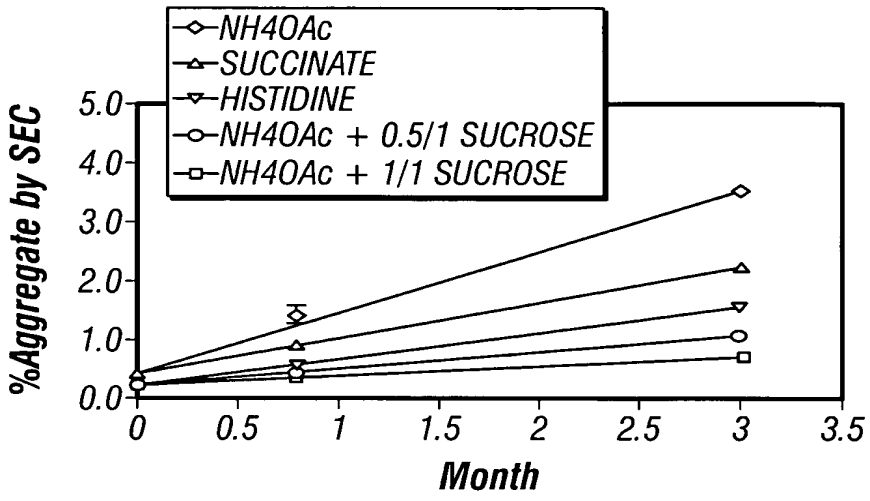
NH4OAc
SUCCINATE
HISTIDINE
NH4OAc + 0.5/1 SUCROSE
NH4OAc + 1/1 SUCROSE
%Aggregate by SEC
5.0
4.0
3.0
2.0
1.0
0.0
0
0.5
1
1.5
2
2.5
3
3.5
Month

FIG. 3

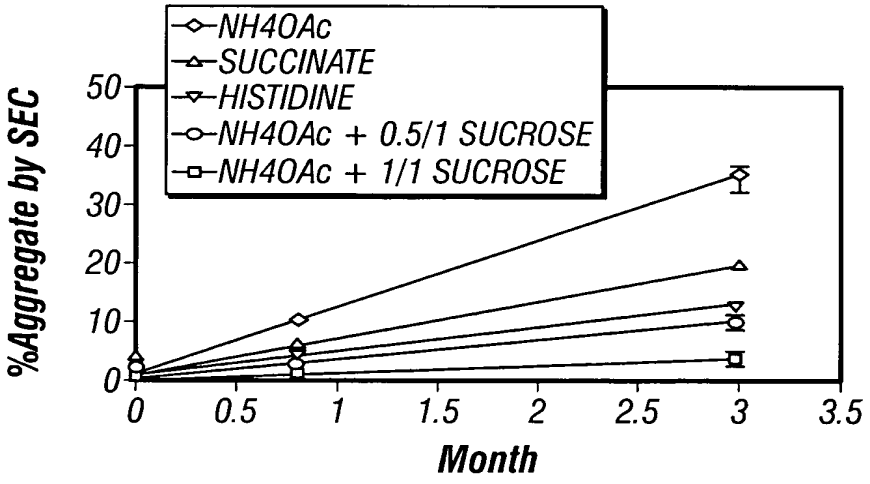
NH4OAc
SUCCINATE
HISTIDINE
NH4OAc + 0.5/1 SUCROSE
NH4OAc + 1/1 SUCROSE
%Aggregate by SEC
50
40
30
20
10
0
0
0.5
1
1.5
2
2.5
3
3.5
Month

FIG. 4

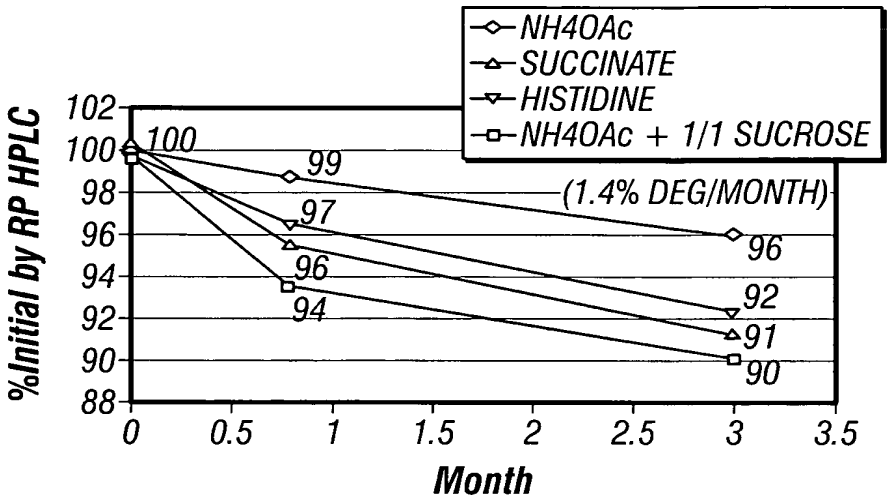
NH4OAc
SUCCINATE
HISTIDINE
NH4OAc + 1/1 SUCROSE
%Initial by RP HPLC
102
100
98
96
94
92
90
88
100
99
97
96
94
96
92
91
90
(1.4% DEG/MONTH)
0
0.5
1
1.5
2
2.5
3
3.5
Month

FIG. 5

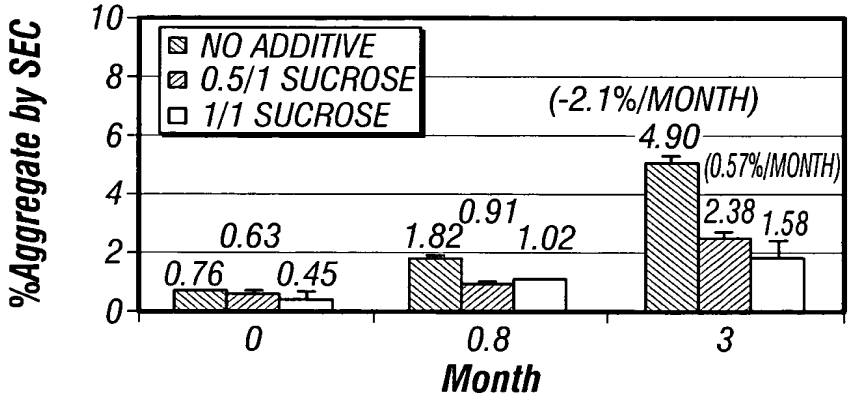
NO ADDITIVE
0.5/1 SUCROSE
1/1 SUCROSE
%Aggregate by SEC
10
8
6
4
2
0
0.76
0.63
0.45
1.82
0.91
1.02
4.90
2.38
1.58
(-2.1%/MONTH)
(0.57%/MONTH)
0
0.8
3
Month

FIG. 6

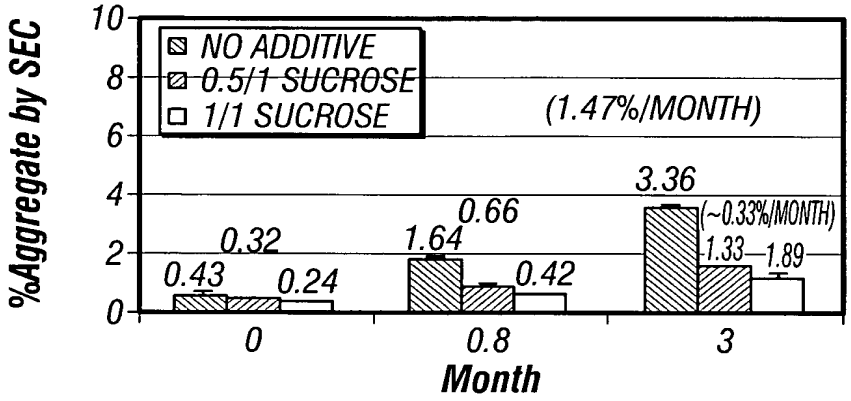
%Aggregate by SEC
10
8
6
4
2
0
NO ADDITIVE
0.5/1 SUCROSE
1/1 SUCROSE
(1.47%/MONTH)
0.43
0.32
0.24
1.64
0.66
0.42
3.36
(~0.33%/MONTH)
1.33
1.89
0
0.8
3
Month

FIG. 7

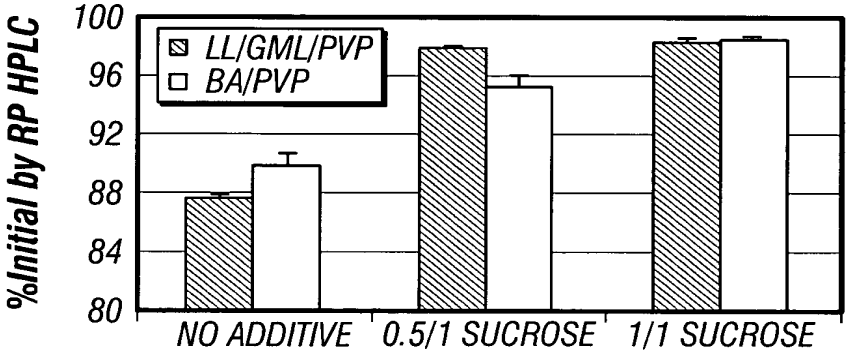
%Initial by RP HPLC
100
96
92
88
84
80
LL/GML/PVP
BA/PVP
NO ADDITIVE
0.5/1 SUCROSE
1/1 SUCROSE

FIG. 8

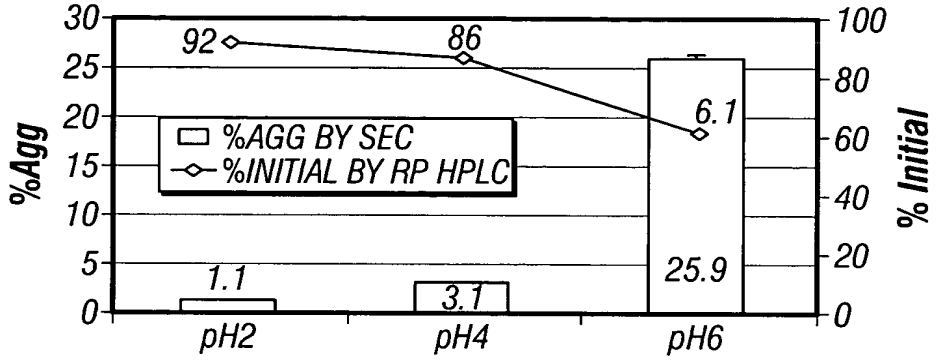

FIG. 9

TABLE 1: *The Stability of PACAP upon Heating at 65°C for 4 hrs*

Suspension Vehicle	Recovery (% Recovery by SEC)	% Initial PACAP by RP-HPLC	% Aggregate by SEC
LL/GML/PVP	95.4 ± 0.5	99.5 ± 0.9	<0.5
BA/PVP	95.5 ± 0.8	99.6 ± 0.1	<0.5
EHL/PVP	96.2 ± 0.5	99.8 ± 0.3	<0.5
PEG400/PVP	91.5 ± 4.9	99.9 ± 0.4	1.1±0.2

* *Samples were reconstituted in 10 mM histidine @ pH6, incubated @ 4°C overnight, filtered, and the filtrate analyzed. n=3 each sample*

TABLE 2: *The Stability of PACAP at 37°C for 17 days*

Suspension Vehicle	***Recovery (% Recovery by SEC)***	***% Initial PACAP by RP-HPLC***	***% Aggregate by SEC***
Lyophilized PACAP	*99 ± 1.3*	*99 ± 0.7*	*0.4±0.03*
LL/GML/PVP	*93 ± 2.6*	*101 ± 0.3*	*0.7±0.03*
EHL/PVP	*96 ± 1.7*	*99 ± 0.2*	*0.8±0.2*
PEG400/PVP	*88*	*99*	*1.8*

** no sample for BA/PVP suspension*

TABLE 3: *The Stability of PACAP at 65°C for 17 days*

Suspension Vehicle	***Recovery (% Recovery by SEC)***	***% Initial PACAP by RP-HPLC***	***% Aggregate by SEC***
Lyophilized PACAP	*95 ± 1.6*	*85 ± 1.9*	*2.9±0.02*
LL/GML/PVP	*93 ± 0.6*	*96 ± 0.4*	*2.4±0.1*
EHL/PVP	*94 ± 0.2*	*95 ± 0.3*	*4.0±0.1*
PEG400/PVP	*87 ± 2.9*	*97 ± 0.5*	*2.9±0.1*

** no sample for BA/PVP suspension*

TABLE 4: *The Estimated Degradation and Aggregation Rates of PACAP at 40° and 60°C*

Excipients	Aggregation (% Aggregate/month)		Total Degradation (% Degradant/month)	
	40°C	60°C	40°C	60°C
Ammonium acetate	1.06	11.2	~3.3	~18.3
Sodium succinate	0.61	6.2	~3.0	~13.3
Histidine	0.45	3.9	~2.7	~11.0
NH4OAc + 0.5/1 sucrose	0.27	3.2	~1.4	~8.5
NH4OAc + 1/1 sucrose	0.16	0.9	1.4	~3.4

* "~" denoted assumed linear increase, see Figure 5

TABLE 5: *The Estimated Degradation and Aggregation Rates of PACAP at 40° and 60°C*

Excipients	Aggregation (% Aggregate Increase /month)		Total Degradation (%Total Degradant Increase/month)	
	40°C	60°C	40°C	60°C
No Additives	1.06	11.2	~3.3	~18.3
Sucrose, 0.5/1 (w/w)	0.27	3.2	~1.4	~8.5
Sucrose, 1/1 (w/w)	0.16	0.9	1.4	~3.4

* "~" denoted approximating to linear increase rate

TABLE 6: *The Stabilization Effect of Sugars at pH2 and pH6 @ 60°C for 2 Months*

Additives	***%Aggregate***		***%Initial PACAP***	
	pH2	*pH6*	*pH2*	*pH6*
No Additive	*1.1*	*26*	*92*	*61*
Methyl MP	*0.8*	*17*	*94*	*73*
Trehalose	*0.7*	*6.3*	*96*	*88*
Sucrose	*24*	*4.2*	*13*	*91*

TABLE 7: *The Stabilization and Additive Stabilization Effects of Histidine, Sucrose, CaC12, and SDS for pH6 PACAP Stored @ 60° for 6 Months*

Additives	***%Aggregate***	***%Initial PACAP***
No Additive	*26*	*61*
Histidine	*4.2*	*87*
CaCl2 (10mM) and Histidine	*1.6*	*92*
Sucrose (0.5/1weight ratio) and Histidine	*1.4*	*92*
Sucrose (0.25/1 weight ratio), CaCl2 (5mM) and Histidine	*1.3*	*92*
SDS (0.02%) and Histidine	*1.8*	*88*

** Histidine concentration was 10 mM for all formulations*

TABLE 8: *The Stabilization and Additive Stabilization Effects of $CaCl_2$ and Histidine, at pH2 and 6 for PACAP Particle Stored @ 60° for 2 months*

Additives	***%Aggregate***	***%Initial PACAP***
pH2 with no Additive	*1.1*	*92*
pH2 with $CaCl_2$	*0.8*	*95*
pH6 with Histidine	*4.2*	*87*
pH6 with $CaCl_2$ and Histidine	*1.6*	*92*

** Histidine concentration of CaCl2 and Histidine were 10 mM*